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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/544,145	12/22/2006	Shyam S. Mohapatra	USF-T192XC1	1541

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/544,145	MOHAPATRA, SHYAM S.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-13,16-21 and 24-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 10-13, 16-21, 24-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/19/2008 has been entered.

Claim Status

Claims 9, 14-15, and 22-23 are cancelled. Claims 10-13, 16-17, 21, and 25-26 are amended. Claims 27-36 are newly added. Claims 1-8, 10-13, 16-21 and 24-26 are under current examination.

Priority

This application claims benefit as a 371 of PCT/US04/04262 (filed 02/13/2004) which claims benefit of 60/319,946 (filed 02/14/2003) and claims benefit of 60/319,956 (filed 02/19/2003). The instant application has been granted the benefit date, 02/14/2003, from the application 60/319,946.

Response to Claim Objections

The examiner withdraws the objection to claim 26 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a

previous claim. The examiner finds the applicant's argument (Remarks, page 6) persuasive.

Response to Claim Rejections - 35 USC § 102

The rejection of claims 1-8, 10-13, 16-21 and 24-26 under 35 U.S.C. 102(e) as being anticipated by Ni et al (US2002/0151009, published 17 October 2002), is withdrawn in response to Applicant's amendment or arguments.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, 10, 21, 25, 28, 29 and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Yu et al. (US2003/0186916, published 2 Oct 2003).

Claim 1 is directed to a particle comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide. Yu et al. teach "a vector for transfecting a eukaryotic cell, comprising a nucleic acid, a nucleic acid binding polymer, a lipid-based vesicle" (page 12, claim 1 and page 3, parag.0014). Yu et al. also teach that "preferred types of

nucleic acid binding polymers include polymers…[such as] chitosan" (page 3, parag.0016).

Claim 5 is directed to a composition comprising a particle and a pharmaceutically acceptable carrier, wherein said particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide. The compositions of Yu et al. are developed for human therapy and are therefore pharmaceutically acceptable.

Claim 10 is directed to a method for delivery and expression of a polynucleotide within a mammal, said method comprising administering a particle to the mammal, wherein the particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide, wherein the polynucleotide is expressed in the mammal. Yu et al. describe their gene therapy compositions as expression systems appropriate for mammals.

Claim 21 is directed to a method for producing the composition of claim 1 by mixing. Yu et al. describe mixing their components.

Claim 25 is directed to the particle of claim 1, wherein said lipid is a cationic lipid. Yu et al. describe various cationic lipids.

Claim 28 is directed to the particle of claim 1, wherein said lipid is a phospholipid. Yu et al. describe various phospholipids lipids including phosphatidylcholine.

Claim 29 is directed to the particle of claim 1, wherein said polynucleotide is surrounded by a monolayer of said lipid. Yu et al. teach lipids may be arranged in monolayers or bilayers (page 6, parag. 38).

Claim 31 is directed to the method of claim 10 wherein the mammal is human. The methods of Yu et al. are used for delivery to humans.

Accordingly, the instant claims are anticipated by Yu et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 10-13, 16-21, 24-28, 30-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hart (Exp. Opin. Ther. Patents. 2000; 10(2): 199-208) in view of Ni et al (US2002/0151009, published 17 October 2002).

Claim 1 is directed to a particle comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide. Hart is a review article which discusses a variety of nucleic acid formulations including lipopolyplexes (which according to Hart are compositions comprising nucleic acids, lipids and cationic polymers) (page 203, section 4). Hart et al. further refers to the polymers as DNA-condensing agents. While Hart does not explicitly teach that chitosan can be used to make the lipopolyplexes, Hart does teach chitosan/DNA nanoparticle compositions (page 203, section 3.4). Ni et al. teach a variety of compositions comprising DNA/ chitosan, and DNA/lipid. Furthermore, Ni et al. teach that their compositions can contain other materials. Ni et al. teach, "formulations and methods of administration that can be employed when the compound comprises a nucleic acid...can be selected from among those described herein below...encapsulation in liposomes" (parag.0410-0411). Ni et al. further teach formulations comprising nucleic acids and biodegradable polymers such as chitosan with combinations and mixtures of other materials (page 113, parag.1032). Ni et al. further teach "formulations comprising compositions of the invention and a biodegradable polymer may also include release rate modification agents" (page 113, col.1034). Ni et al. teach that their controlled

release formulations may also include release-rate modification agents and/or pore-forming agents such as fatty acids (lipids) (page 56, parags. 0537-0538). Ni et al. clearly suggests a particle comprising (1) nucleic acids, (2) the biodegradable polymer, chitosan, and (3) the release-rate modification agent, fatty acids (also known as lipids).

Claim 2 is directed to the particle of claim 1, wherein said particle is a nanoparticle. It is well established in the art that delivery of nucleic acids in particles comprising substances such as chitosan or liposomes is in the nano-scale. Hart discloses nanosized particles of chitosan/DNA (page 203, section 3.4).

Claim 3 is directed to the particle of claims 1, wherein said polynucleotide encodes a cytokine. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 4 is directed to the particle of claim 1, wherein said polynucleotide encodes interferon gamma. Ni et al. teach interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 5 is directed to a composition comprising a particle and a pharmaceutically acceptable carrier, wherein said particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide. Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407). Hart teaches lipopolyplexes and includes

teachings of compositions comprising the polymer, chitosan, suggestive of the instant claim.

Claim 6 is directed to the composition of claim 5, wherein said particle is a nanoparticle. It is well established in the art that delivery of nucleic acids in particles comprising substances such as chitosan or liposomes is in the nano-scale. Hart discloses nanosized particles of chitosan/DNA (page 203, section 3.4).

Claim 7 is directed to the composition of claim 5, wherein said polynucleotide encodes a cytokine. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407).

Claim 8 is directed to the composition of claim 5, wherein said polynucleotide encodes interferon gamma. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407).

Claim 10 is directed to a method for delivery and expression of a polynucleotide within a mammal, said method comprising administering a particle to the mammal,

wherein the particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide, wherein the polynucleotide is expressed in the mammal. Ni et al. teach, methods of treatment using gene therapy wherein non-replicating DNA sequences can be introduced into the cells of a mammal and provide production of the desired polypeptide for periods of up to six months," (page 124, parag.1124).

Claim 11 is directed to the method of claim 10, wherein said particle is a nanoparticle. It is well established in the art that delivery of nucleic acids in particles comprising substances such as chitosan or liposomes is in the nano-scale.

Claim 12 is directed to the method of claim 10, wherein the polynucleotide encodes a cytokine. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 13 is directed to the method of claim 10, wherein the polynucleotide encodes interferon gamma. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 16 is directed to the method of claim 10, wherein the particle is administered within a composition comprising a pharmaceutically acceptable carrier. Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407).

Claim 17 is directed to a method for enhancing interferon-gamma expression to regulate the production of cytokines secreted by T-helper type 2 (Th2) cells, said method comprising administering an effective amount of a particle to a mammal, wherein the particle comprises chitosan, or a chitosan derivative, a lipid, and a polynucleotide encoding interferon-gamma and wherein the polynucleotide is expressed, producing interferon-gamma in the mammal. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. also teach "administration of polynucleotides…of the present invention…[modulate] proliferation, differentiation, or chemotaxis of T-cells" (page 59-60, parag.0580).

Claim 18 is directed to the method of claim 17, wherein the mammal is human. Ni et al. teach that their compositions could be used to treat humans (page 58, parag. 0563).

Claim 19 is directed to the method of claim 17, wherein the mammal is suffering from asthma. Ni et al. teach, "compositions of the invention may be used as agents for immunological disorders including…asthma." (page 7, parag.0086).

Claim 20 is directed to the method of claim 17, wherein the particle is administered to the respiratory tract of the mammal. Ni et al. teach aerosol administration of the compositions (page 58, parag. 0561).

Claim 21 is directed to a method for producing a particle comprising a complex of chitosan, or a chitosan derivative and a polynucleotide, said method comprising mixing the polynucleotide, the lipid, and the chitosan or chitosan derivative, to form the particle. Ni et al. teach formulations comprising nucleic acids and chitosan and combinations and mixtures of other materials (page 113, parag. 1032). Ni et al. teach creating the particles through a process of mixing (page 44, parag.0418).

Claim 24 is directed to the method of claim 10, wherein the particle is administered intranasally. Ni et al. teach intranasal administration (page 43, parag.0411).

Claim 25 is directed to the particle of claim 1, wherein the lipid is a cationic lipid or phospholipid. Ni et al. teach certain embodiments wherein the polynucleotide is complexed with cationic lipids (page 55, parag.0535).

Claim 26 is directed to the particle of claim 1, wherein the particle comprises chitosan. Ni et al. teaches particles comprising chitosan. Hart teaches lipopolyplexes and includes teachings of compositions comprising the polymer, chitosan, suggestive of the instant claim.

Claim 27 is directed to the particle of claim 1, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of a component of a composition would be an obvious variant.

Claim 28 is directed to the particle of claim 1, wherein said lipid is a phospholipid. Hart describes making lipoplexes that incorporate phosphatidylcholine. This would therefore be obvious to incorporate such phospholipids into the lipopolyplexes.

Claim 30 is directed to the method of claim 10, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of a component of a composition would be an obvious variant.

Claim 31 is directed to the method of claim 10 wherein the mammal is human. Ni et al. teach "therapeutic methods useful for ...treating...disorder related to these novel human polypeptides" (page 1, parag.0002).

Claim 32 is directed to the method of claim 10, wherein said particle is administered to the respiratory tract of the mammal. Ni et al. teach treating lung.

Claim 33 is directed to the method of claim 17, wherein the particle is administered intranasally. Ni et al. teach intranasal delivery.

Claim 34 is directed to the method of claim 17, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of a component of a composition would be an obvious variant.

Claim 35 is directed to the method of claim 21, wherein said polynucleotide encodes interferon gamma. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. also teach "administration of polynucleotides...of the present invention...[modulate] proliferation, differentiation, or chemotaxis of T-cells" (page 59-60, parag.0580).

Claim 36 is directed to the method of claim 21, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of any component of a composition would be an obvious variant.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to combine the teachings of Hart and Ni et al. to produce a lipopolyplex composition of chitosan, or a chitosan derivative; a lipid; and a polynucleotide for delivery of a polynucleotide to a mammal.

The person of ordinary skill in the art would have been motivated to use chitosan in the lipopolyplexes of Hart because chitosan well known as biocompatible, non-toxic, cationic polymer used in polymer/DNA complexes. Therefore, it is an obvious substitution within the lipopolyplex composition.

An artisan would have expected success, because formulating polylipoplexes were known in the art prior to the instant application.

Therefore the compositions and methods as taught by Hart in view of Ni et al. would have been *prima facie* obvious over the compositions and methods of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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